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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,013	04/28/2005	Koushi Nakano	Saeg153.002APC	1676

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EXAMINER	
NOBLE, MARCIA STEPHENS	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 07/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/533,013	NAKANO ET AL.	
	Examiner	Art Unit	
	Marcia S. Noble	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *18 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *13-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *4/28/05* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/22/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-12, in the reply filed on 4/18/06 is acknowledged.

Claims 13-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/18/06.

Claims 1-12 are under consideration.

Priority

2. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant claims priority to PCT/JP03/13743 (f.d.- 10/28/03). Applicant has complied with conditions for receiving the benefit of an earlier filing date.

Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d) prior to declaration of an interference, a translation of the foreign application should be submitted under 37 CFR 1.55 in reply to this action.

Although priority papers have been submitted in the instant case, a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Information Disclosure Statement

3. The information disclosure statement (IDS) filed on 7/22/05. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. However, Reference Cite No. 7 was only partially considered because only a partial English translation and an English abstract was provided.

Claim Rejections - 35 USC § 112, 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of Enablement

4. Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a non-human animal model exhibiting prostate tissue damage characteristic of chronic nonbacterial prostatitis and a lower urinary tract disorder characteristically observed in chronic nonbacterial prostatitis wherein in the animal model is prepared by injection of hydrochloric acid (HCl), wherein the HCl concentration ranges from 0.1 N to 0.4 N, a method of using said nonbacterial prostatitis non-human animal model comprising administering a test substance and determining if it alleviates prostate tissue damage or lower urinary tract disorder symptoms, and a method of making said non-human prostatitis animal model comprising injecting HCl beneath the prostatic capsule wherein the HCl is between 0.1 N and 0.4 N, does not

reasonably provide enablement for a nonbacterial prostatitis animal model produced using any concentration of HCl. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make or use the claimed invention, if not, whether an artisan would require undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue".

Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

In example 1, the specification teaches a method comprising of exteriorizing the prostate of a rat and injecting 100 μl of 0.1, 0.2, or 0.4 N HCl in saline beneath the prostatic capsule of the right lateral lobe (p. 35 lines 25-35). The specification also

teaches that rats treated with the localized injection of 0.1, 0.2, or 0.4 N HCl developed severe tissue damage exhibiting coagulation necrosis at the lumen wall affecting as far as a portion of the prostate tissue near the urethra and partial tissue disorder (tigrolysis) was observed in nerves cells attached to or present in the prostate (p. 38, lines 23-29). With regards to the urethral or bladder tissues, no evidence of tissue damage extending from the prostate via the urethra was present suggesting the damage was substantially only in the prostate (P. 38, lines 30-35). In terms of urinary tract disorder the specification teaches,

parametric values for the bladder function in the test groups differ depending on the concentration of hydrochloric acid injected, purpose-built nonbacterial prostatitis animal models can be prepared by adjusting the concentration of hydrochloric acid (p. 42, line 33 to p. 43 line 2).

The specification also teaches the prostate to body weight and the bladder to body weigh ratios increase as the concentration of HCl increases and suggests,

It can therefore be presumed that, in relation to the concentration of hydrochloric acid injected, the extent of organic change in the prostate tissue as well as the effect on the nervous system intrinsic to the prostate change, and the change in the extent of lower urinary tract disorders (change in the volume of residual urine) is reflected in the weight of the bladder. (p. 43, lines 28 to 34)

Overall, these results suggest that the range of HCl concentrations that they used are capable of producing a nonbacterial prostatitis model with characteristics of prostate tissue damage and lower urinary tract disorder and that the severity of the

claimed phenotype is dependent upon the concentration of the HCl. However, the specification dose not teach the phenotypes and the phenotype severity for concentrations of HCl outside of this range. HCl is well established as an agent capable of extensive tissue damage and destruction. Treatments with concentrations of HCl that are too high, would result in extensive destruction of the tissue, therefore an artisan could not use an animal model of prostatitis with extensive tissue damage as a model because the tissues would be well beyond repair or any treatment. Similarly, the use of too little HCl has the potential of not inducing any pathological effect and therefore, there would be no phenotype for an artisan to use to address treatment. Therefore, given that not any concentration of HCl will produce the desired nonbacterial prostatitis model phenotype, and the specification is not enabling for the use of any HCl concentration as claimed, the specification provides enabling disclosure only for the use of HCl concentrations demonstrated to provide the desired phenotype as disclosed.

Claim Rejections - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "about" in claim 5 is a relative term that renders the claim indefinite. The term "about" is not defined by the claim, the specification does not provide a

standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In the instant case, about 4 days to about 1 week, could be suggestive of anytime period to an artisan as long as symptoms of prostatitis appear.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lang et al (of record; 2000), Keetch et al (of record, 1994), Fulmer et al (of record;

2000), Robinette (of record, 1988), and Royston D (Acta anaesthesiologica Scandinavica 30(7):abstract, 1986), in view of Goto (of record; 1988).

The instant invention is drawn to a nonbacterial prostatitis rat model exhibiting prostate tissue damage and lower urinary tract disorder characteristic of human chronic nonbacterial prostatitis wherein said prostatitis rat model is produced by injecting HCl into the dorsolateral prostatic lobe and rearing the rat about 4 days to one week following injection until the rat develops symptoms of prostatitis and lower urinary tract disorder. Narrowing embodiments specify that the urinary disorder be a urinary storage disorder posing symptoms of pollakiuria, urinary incontinence, or reduced effective bladder capacity. The instant invention is also drawn to a method for screening for a treatment substance comprising administering a test substance to the nonbacterial prostatitis rat model and examining the test substance for ameliorating prostate tissue damage or a lower urinary tract disorder displaying at least one of the above described symptoms.

Lang et al teach a method of producing a rat model of experimentally induced abacterial prostatitis comprising the delivery of dinitrobenzenesulfonic acid (DNBS) in 50% ethanol into the rat ventral prostate (p. 202, col 1, par 2). Through morphological analysis, treated prostates had significantly increased symptoms of inflammation (ie increased edema, congestion, and hyperemia (Fig 1 and par bridging 202-203). Histological analysis taught increased edema, leukocyte infiltration, and hemorrhage (figure 2 and col 1, par 1 on p. 203). All of these symptoms are indicative of abacterial prostatitis. Lang et al also teaches that the etiology of abacterial prostatitis is unknown

and has lead to the need and development of a number of animal models to study the multiple hypothesized causes of nonbacterial prostatitis (p. 204, col 1, par 1 of discussion). Lang et al teach that other chemical irritants are also used to produced inflammation animal models as well (p. 205, last par). Because the etiology of abacterial prostatitis is unknown, several other non-specific irritants that would induce idiopathic inflammation can be used to incite inflammatory responses leading to prostatitis. These teachings suggest that other irritants and agents can be used to insight inflammatory responses and prostatitis or other organs as well. Keetch et al, Fulmer et al, and Robinette et al further support these teachings by using other irritants or inflammatory agents, such as LPS, prostate extracts, testosterone, to induce symptoms of prostatitis (see abstracts) and ultimately demonstrate that it is the inflammatory or irritant nature of the agent that is important to inducing that prostatitis. However, neither Lang et al., Keetch et al., Fulmer et al., nor Robinette et al. does not specifically contemplate the use of HCl as an irritant to induce prostatitis.

However, both Royston et al and Goto et al. teach the use of the non-specific irritant HCl to induce an idiopathic inflammation in tissues to which HCl has been administered. Royston et al teaches instillation of HCl to the lung of a rat that induces edema and severe inflammation. Royston et al specifically state that HCl will induce a severe inflammatory response in tissues. Goto et al also teaches the use of HCl to induce prostatitis by administering HCl through the vas deferens further demonstrating the use of HCl in developing prostatitis animal models.

At the time of the invention, it would have been obvious to an artisan of ordinary skill to make a rat model of abacterial chronic prostatitis by injection of an irritant as taught by Lang et al. using HCl as the irritant as taught by both Royston et al. and Goto et al. An artisan would have been motivated the use HCl as the irritant to induce abacteria prostatitis in a rat model as described by Lang et al because HCl is a nonspecific irritant that induces severe idiopathic inflammation as taught by Royston et al. Furthermore, it also would have been obvious to an artisan of ordinary skill to use of HCl to produce a nonbacterial prostatitis rat model with a reasonable expectation of success because HCl had been previously used in the production of prostatitis model as taught by Goto et al. and HCl was demonstrated to work as a general, nonspecific inducer of inflammation in other tissues.

The narrowing embodiments of the instantly claimed invention are also taught by art. Lang et al also teach that some of the rats developed severe prostatitis, prostatic urethral occlusion, and urinary retention (p. 203, col 1, lines 8-11), which would be considered a lower urinary tract disorder as well as bladder disorder. Inherently this would also result in an increase in bladder weight to body weight (claim 2) and potentially reduced effective bladder capacity (claims 3) as claimed. Overall, Lang et al teaches that a more severe case of prostatitis will lead to lower urinary tract disorders. This is similar to what is seen in human prostatitis as well.

The instant claims contemplate the use of their disclosed prostatitis model in screening for therapeutic agents. Overall, if an animal model is developed for a disease, it would be obvious to use it to develop treatments and determine therapeutic

agents using methodologies that are already well established in the art. Royston is an example of this, wherein they administer indoprofen to their rodent model and determine effectiveness of this agent to alleviate the inflammatory response.

Lang et al does not specifically teach rearing and the presence of symptoms between "about 4 days to about 1 week" as claimed. However, the "about" is suggestive of variability in the onset of symptoms and development of symptoms is the more implicit action than the actual relative time in which the symptoms appear. Therefore, because "about" is relative and because timing of onset of symptoms can be variable, the 24 hours and the 48 hours onset of symptoms taught by Lang et al is within the relative interpreted of "about 4 days to about 1 week" for rearing to obtain symptoms.

Lang et al also fails to teach injection into the dorsolateral lobe. However, Lang et al. and the art of record demonstrate that administering to a specific area of the prostate does not limit its impact to other areas of the prostate. For example, delivery to the vas deference of HCl still resulted in prostatic damage as evidenced by Goto et al (of record).

Conclusions and Relevant Art

7. The instantly claimed methods and produced animal model of prostatitis was found to only be partially enabled by the specification because the non-specific nature of damage and inflammation caused by administering HCl to a the prostate could be damaging beyond treatment or service as a model for prostatitis. Therefore the instant

invention would only be enable for the range of HCl concentration disclosed to produce the prostatitis phenotype disclosed.

The instant invention as claims was also deemed obvious. Because the etiology of abacterial prostatitis is unknown and others are using non-specific irritants to induce prostatitis as taught by Lang et al., it would be obvious to an artisan to use HCl to induce prostatitis because HCl is well established as an irritant causing tissue damage and induces inflammation.

Goto et al. seems to be the closest art to the instantly claimed invention. However, this art is not heavily relied upon in the instant rejections because only a partial English translation was provided. Examiner intends to obtain Goto et al. for translation for further examination.

8. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marcia S. Noble whose telephone number is (571) 272-5545. The examiner can normally be reached on M-F 9 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Marcia S. Noble

Valerie Bertoglio
Patent Examiner